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CHAKRABARTI, ARUN K

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/424,629	Applicant(s) Simon Foote et al.
	Examiner Arun Chakrabarti	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 24, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-18 and 24-32* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-18 and 24-32* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 24, 2003 has been entered.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

3. Claims 1-5 and 24-28 are rejected under 35 U.S.C. 102 (e) as being anticipated by Kamb (U.S. Patent 5,869,242) (February 9, 1999).

Kamb teaches a method of detecting a difference of one or more nucleotides between a nucleic acid molecule to be tested and a reference nucleic acid molecule and identifying a mutation (Abstract) , the method comprising:

subjecting the test nucleic acid molecule to base specific cleavage to generate oligonucleotide fragments (Claims 1-3 and 5 and Example IV, Column 6, line 50 to column 8, line 37);

separating the resulting oligonucleotide fragments based on mass by MALDI-TOF MS to produce a fingerprint of the oligonucleotide fragments comprising one or more peaks wherein a peak represents the mass of each fragment (Tables II and III and Example IV, Column 6, line 50 to column 8, line 37); and

identifying an altered peak relative to a reference nucleic acid molecule subjected to the same procedure wherein the presence of an altered peak is indicative of a difference of one or more nucleotides in the tested nucleic acid molecule (Claims 1 and 3 and Table II).

Kamb teaches a method wherein the nucleic acid molecule to be tested is amplified by a PCR prior to base specific cleavage (Column 4, lines 36-46 and Column 7, lines 39-54).

Kamb teaches a method wherein the base specific cleavage results in oligonucleotide fragments of from about 2 bases to about 1000 bases (Table III).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 6-7 and 29-30 are rejected under 35 U.S.C. 103 (a) over Kamb (U.S. Patent 5,869,242) (February 9, 1999) in view of Sutherland et al. (U.S. Patent 5,985,619) (November 16, 1999).

Kamb teaches the method of claims 1-5 and 24-28 as described above.

Kamb does not teach the method wherein the base specific cleavage is uracil specific and mediated by uracil-N-glycosylase.

Sutherland et al. teach the method wherein the base specific cleavage is uracil specific and mediated by uracil-N-glycosylase (Column 9, lines 4-29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the mass spectrometry to assess DNA sequence polymorphisms of Kamb, since Sutherland et al. state, "The glycosylase useful in the present

invention are those that specifically cleave unconventional bases, i.e., bases other than A,G,C or T in DNA and A,G,C and U in RNA. Glycosylases that specifically cleave unconventional bases such as N-& methylguanine, 3-methyladenosine, uracil and hypoxanthine are known to one of ordinary skill in the art. Preferred glycosylases include uracil N-glycosylase (UNG), hypoxanthine-DNA glycosylase, and 3-methyladenine-DNA glycosylases I and II. The most preferred glycosylase in accordance with present invention is UNG. UNG is commercially available (Column 9, lines 4-19)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the mass spectrometry to assess DNA sequence polymorphisms of Kamb in order to improve the sequencing of nucleic acids containing unconventional bases. An ordinary practitioner would have been motivated to combine and substitute the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the mass spectrometry to assess DNA sequence polymorphisms of Kamb in order to achieve the express advantages noted by Sutherland et al., of a preferred glycosylase UNG which is commercially available and useful to specifically cleave unconventional bases.

6. Claims 10, and 14 are rejected under 35 U.S.C. 103 (a) over Kamb (U.S. Patent 5,869,242) (February 9, 1999) in view of Koster (U.S. Patent 6,074,823) (June 13, 2000).

Kamb teaches the method of claims 1-5 and 24-28 as described above.

Kamb does not teach the method of using a computer capable of controlling a method of detecting mutation by MALDI-TOF MS.

Koster teach the method of using a computer capable of controlling a method of detecting mutation by MALDI-TOF MS (Column 5, lines 22-35).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a computer capable of controlling a method of detecting mutation by MALDI-TOF MS of Koster into the mass spectrometry to assess DNA sequence polymorphisms of Kamb, since Koster states, "An additional advantage of mass spectrometric sequencing is that the identified masses can be registered automatically by a computer and, by adding the time coordinate, automatically aligned to sequences. Since the sequences so determined are memorized (i.e., saved to disk or resident in the computer memory), appropriate existing computer programs operating in a multitasking environment can be searching in the "background" (i.e., during continuous generation of new sequence data by the exonuclease mass spectrometric sequencer) for overlaps and generate contiguous sequence information which, via a link to a sequence data bank, can be used in homology searches, etc (Column 5, lines 22-35)." By employing scientific reasoning, an ordinary artisan would have combined and substituted a computer capable of controlling a method of detecting mutation by MALDI-TOF MS of Koster into the mass spectrometry to assess DNA sequence polymorphisms of Kamb in order to improve the sequencing of nucleic acids by automated procedures. An ordinary practitioner would have been motivated to combine and substitute a computer capable of controlling a method of detecting mutation by MALDI-TOF MS of Koster into the mass spectrometry to assess DNA sequence polymorphisms of Kamb in order to achieve the express advantages noted by Koster, of

mass spectrometric sequencing by which the identified masses can be registered automatically by a computer and, by adding the time coordinate, automatically aligned to sequences and since the sequences so determined are memorized (i.e., saved to disk or resident in the computer memory), appropriate existing computer programs operating in a multitasking environment can be searching in the "background" (i.e., during continuous generation of new sequence data by the exonuclease mass spectrometric sequencer) for overlaps and generate contiguous sequence information which, via a link to a sequence data bank, can be used in homology searches, etc

7. Claims 8-9, 11-13, and 31-32 are rejected under 35 U.S.C. 103 (a) over Kamb (U.S. Patent 5,869,242) (February 9, 1999) in view of Caprioli (U.S. Patent 5,808,300) (September 15, 1998).

Kamb teaches the method of claims 1-5 and 24-28 as described above.

Kamb does not teach the method of subjecting fragmentation products to further separation by the post source decay method.

Caprioli teaches the method of subjecting fragmentation products to further separation by post source decay method (Column 3, lines 9-11).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a further separation by post source decay method of Caprioli into the mass spectrometry to assess DNA sequence polymorphisms of Kamb , since Caprioli states, "The use of post-source decay techniques is shown in order to obtain sequence verification (Column 3, lines 9-11)." By employing scientific reasoning, an ordinary

artisan would have combined and substituted a further separation by post source decay method of Caprioli into the mass spectrometry to assess DNA sequence polymorphisms of Kamb in order to improve the sequencing of nucleic acids. An ordinary practitioner would have been motivated to combine and substitute a further separation by post source decay method of Caprioli into the mass spectrometry to assess DNA sequence polymorphisms of Kamb in order to achieve the express advantages, as noted by Caprioli, of a method which is used in order to obtain sequence verification.

8. Claims 16 is rejected under 35 U.S.C. 103 (a) over Kamb (U.S. Patent 5,869,242) (February 9, 1999) in view of Koster (U.S. Patent 6,074,823) (June 13, 2000) further in view of Sutherland et al. (U.S. Patent 5,985,619) (November 16, 1999).

Kamb in view of Koster teach the method of claims 1-5, 10, 14 and 24-28 as described above.

Kamb in view of Koster do not teach the method wherein the base specific cleavage is uracil specific and mediated by uracil-N-glycosylase.

Sutherland et al. teach the method wherein the base specific cleavage is uracil specific and mediated by uracil-N-glycosylase (Column 9, lines 4-29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Koster, since Sutherland et al. state, "The

glycosylase useful in the present invention are those that specifically cleave unconventional bases, i.e., bases other than A,G,C or T in DNA and A,G,C and U in RNA. Glycosylases that specifically cleave unconventional bases such as N-& methylguanine, 3-methyladenosine, uracil and hypoxanthine are known to one of ordinary skill in the art. Preferred glycosylases include uracil N-glycosylase (UNG), hypoxanthine-DNA glycosylase, and 3-methyladenine-DNA glycosylases I and II. The most preferred glycosylase in accordance with present invention is UNG. UNG is commercially available (Column 9, lines 4-19)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Koster in order to improve the sequencing of nucleic acids containing unconventional bases. An ordinary practitioner would have been motivated to combine and substitute the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Koster in order to achieve the express advantages noted by Sutherland et al., of a preferred glycosylase UNG which is commercially available and useful to specifically cleave unconventional bases.

9. Claims 15 is rejected under 35 U.S.C. 103 (a) over Kamb (U.S. Patent 5,869,242) (February 9, 1999) in view of Caprioli (U.S. Patent 5,808,300) (September 15, 1998)further in view of Sutherland et al. (U.S. Patent 5,985,619) (November 16, 1999).

Kamb in view of Caprioli teach the method of claims 1-5, 8-9, 11-13, 24-28 and 31-32 as described above.

Kamb in view of Caprioli do not teach the method wherein the base specific cleavage is uracil specific and mediated by uracil-N-glycosylase.

Sutherland et al. teach the method wherein the base specific cleavage is uracil specific and mediated by uracil-N-glycosylase (Column 9, lines 4-29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Caprioli, since Sutherland et al. state, "The glycosylase useful in the present invention are those that specifically cleave unconventional bases, i.e., bases other than A,G,C or T in DNA and A,G,C and U in RNA. Glycosylases that specifically cleave unconventional bases such as N-& methylguanine, 3-methyladenosine, uracil and hypoxanthine are known to one of ordinary skill in the art. Preferred glycosylases include uracil N-glycosylase (UNG), hypoxanthine-DNA glycosylase, and 3-methyladenine-DNA glycosylases I and II. The most preferred glycosylase in accordance with present invention is UNG. UNG is commercially available (Column 9, lines 4-19)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Caprioli in order to improve the sequencing of nucleic acids

containing unconventional bases. An ordinary practitioner would have been motivated to combine and substitute the uracil specific base cleavage mediated by uracil-N-glycosylase of Sutherland et al. into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Caprioli in order to achieve the express advantages noted by Sutherland et al., of a preferred glycosylase UNG which is commercially available and useful to specifically cleave unconventional bases.

10. Claims 17-18 are rejected under 35 U.S.C. 103 (a) over Kamb (U.S. Patent 5,869,242) (February 9, 1999) in view of Koster (U.S. Patent 6,074,823) (June 13, 2000) further in view of Caprioli (U.S. Patent 5,808,300) (September 15, 1998).

Kamb in view of Koster teach the method of claims 1-5, 10, 14 , and 24-28 as described above.

Kamb in view of Koster do not teach the method of subjecting fragmentation products to further separation by the post source decay method.

Caprioli teaches the method of subjecting fragmentation products to further separation by post source decay method (Column 3, lines 9-11).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a further separation by post source decay method of Caprioli into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Koster, since Caprioli states, "The use of post-source decay techniques is shown in order to obtain sequence verification (Column 3, lines 9-11)." By

employing scientific reasoning, an ordinary artisan would have combined and substituted a further separation by post source decay method of Caprioli into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Koster in order to improve the sequencing of nucleic acids. An ordinary practitioner would have been motivated to combine and substitute a further separation by post source decay method of Caprioli into the computerized mass spectrometry to assess DNA sequence polymorphisms of Kamb in view of Koster in order to achieve the express advantages, as noted by Caprioli, of a method which is used in order to obtain sequence verification.

Response to Arguments

11. Applicant's arguments filed on February 24, 2003, have been fully considered but they are not persuasive.

Applicant argues that Kamb reference should be withdrawn from 102 (e) rejection because Kamb does not teach "base specific cleavage" and it teaches only "sequence-specific cleavage".Applicant argues that Kamb reference does not teach the "base specific cleavage" of the claimed invention. Applicant argues that the word "base specific cleavage" was not found in Kamb reference and only the word "sequence-specific cleavage" is found. Applicant argues that because Kamb has a preferred embodiment of "sequence-specific cleavage", Kamb is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure

or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Kamb has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Kamb reference uses "sequence-specific cleavage", the property of "base specific cleavage" is inherently present in this chemically and structurally identical molecule. For example, Kamb clearly teaches that nucleic acids can be digested with uracil-N-glycosidase (Column 4, lines 39-41). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)". In this case, any restriction enzymes can be used for "base specific cleavage". This rejection is also based on the fact that the applicant broadly defined the nucleic acid cleavage as disclosed on page 11 of the specification, "The nucleic acid may be cleaved by a range of chemical molecules including enzymes (line 7)" and "however, a range of enzymes may be employed (lines 9-10)". This broad disclosure in the specification encompasses any nucleic acid cleaving enzyme.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that Sutherland et al. reference has different motivation to use uracil-N-glycosylase, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In view of the response to argument, all previous 102(e) as well as 103(a) rejections are hereby properly maintained.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 746-4979. Any inquiry of a general nature or relating to the status of this

application or proceeding should be directed to the Group analyst Chantae Dessau, who can be reached at (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

March 10, 2003

ARUN K. CHAKRABARTI
PATENT EXAMINER